

Claims

We claim:

1. A method for isolating a nucleic acid molecule fragment comprising at least a portion of a gene, comprising:
 - a) stimulating at least one cell or at least one nucleus with radiation;
 - b) cross-linking at least one transcription factor to a nucleic acid molecule in said at least one cell or at least one nucleus with formaldehyde, forming at least one transcription factor-nucleic acid molecule complex;
 - b) fragmenting said nucleic acid molecule to form at least one transcription factor-nucleic acid molecule fragment complex; and
 - d) isolating the nucleic acid molecule fragment from said at least one transcription factor-nucleic acid molecule fragment complex to form at least one isolated nucleic acid molecule fragment;wherein said at least one isolated nucleic acid molecule fragment comprises at least a portion of the first exon of a gene whose expression is modulated by said transcription factor; further wherein said at least one isolated nucleic acid molecule fragment comprises at least one transcription factor binding site that is operably linked or in close proximity to said first exon of a gene.
2. A method for isolating at least one nucleic acid molecule fragments that comprises a portion of a gene regulated by a transcription factor, comprising:
 - a) cross-linking at least one transcription factor to at least one nucleic acid molecule in at least one cell or at least one nucleus, forming at least one transcription factor-nucleic acid molecule complex;
 - b) fragmenting said at least one nucleic acid molecule to form at least one transcription factor-nucleic acid molecule fragment complex; and
 - c) isolating at least one nucleic acid molecule fragment from said at

least one transcription factor-nucleic acid molecule fragment complex to obtain at least one isolated nucleic acid molecule fragment;

wherein said at least one isolated nucleic acid molecule fragment comprises at least a portion of the first exon of a gene whose expression is modulated by said transcription factor; further wherein said at least one isolated nucleic acid molecule fragment comprises at least one transcription factor binding site that is operably linked or in close proximity to said first exon of a gene.

3. The method of claim 2, wherein said at least one nucleic acid molecule comprises genomic DNA.
4. The method of claim 2, wherein said transcription factor is selected from the group consisting of leucine zipper factors, helix-loop-helix factors, helix-loop-helix/leucine zipper factors, NF-1 factors, RF-X factors, bHSH factors, Cys4 zinc finger of nuclear receptor factors, diverse Cys4 zinc finger factors, Cys2His2 zinc finger factors, Cys6 cysteine-zinc cluster factors, Homeo domain factors, paired box factors, fork head/winged helix factors, heat shock factors, tryptophane cluster factors, TEA domain factors, RHR factors, p53 factors, MADS box factors, beta-barrel alpha-helix factors, TATA-binding factors, HMG factors, heteromeric CCAAT factors, Grainyhead factors, cold-shock domain factors, Runt factors, copper fist factors, HMGI(Y) factors, STAT factors and pocket domain factors.
5. The method of claim 2, wherein said transcription factor is Egr-1.
6. The method of claim 2, wherein said at least one cell or at least one nucleus is at least one cell.
7. The method of claim 6, wherein said at least one cell is a living cell.
8. The method of claim 7, wherein said at least one living cell is irradiated prior to

said cross-linking.

9. The method of claim 2, wherein said cross-linking is performed using formaldehyde.
10. The method of claim 2, further comprising amplifying said at least one nucleic acid molecule fragment.
11. A method for identifying one or more cDNA molecules that correspond to one or more genes regulated by a transcription factor, comprising:
 - a) cross-linking at least one transcription factor to at least one nucleic acid molecule in at least one cell or at least one nucleus, forming one or more transcription factor-nucleic acid molecule complexes;
 - b) fragmenting said at least one nucleic acid molecule to form one or more transcription factor-nucleic acid molecule fragment complexes;
 - c) isolating one or more nucleic acid molecule fragments from said one or more transcription factor-nucleic acid molecule fragment complexes to form one or more isolated nucleic acid molecule fragments;
 - d) combining said one or more isolated nucleic acid molecule fragments with either:
 - 1) a cDNA library, or
 - 2) cDNA obtained by reverse transcription of a population of RNA molecules, to form a mixture comprising isolated nucleic acid molecule fragment/cDNA complexes; and
 - e) amplifying one or more cDNAs that binds with said one or more isolated nucleic acid molecule fragment using said one or more nucleic acid molecule fragments as primers to obtain one or more isolated cDNA molecules, said one or more isolated cDNA molecules comprising at least a portion of a gene operably linked to or in close proximity to a nucleic acid sequence that binds with at least one

transcription factor; and

f) identifying said one or more cDNAs by either:

- 1) sequencing said one or more cDNAs and comparing said sequence to the sequences of DNA molecules of known sequence, or
- 2) hybridizing said one or more cDNAs to one or more nucleic acid molecules corresponding to known genes or nucleic acid sequences.

12. The method of claim 11, wherein said amplifying comprises cloning said one or more isolated cDNA molecules in at least one vector.
13. The method of claim 11, wherein said at least one nucleic acid molecule comprises genomic DNA.
14. The method of claim 11, wherein said transcription factor is selected from the group consisting of leucine zipper factors, helix-loop-helix factors, helix-loop-helix/leucine zipper factors, NF-1 factors, RF-X factors, bHSH factors, Cys4 zinc finger of nuclear receptor factors, diverse Cys4 zinc finger factors, Cys2His2 zinc finger factors, Cys6 cysteine-zinc cluster factors, Homeo domain factors, paired box factors, fork head/winged helix factors, heat shock factors, tryptophane cluster factors, TEA domain factors, RHR factors, p53 factors, MADS box factors, beta-barrel alpha-helix factors, TATA-binding factors, HMG factors, heteromeric CCAAT factors, Grainyhead factors, cold-shock domain factors, Runt factors, copper fist factors, HMGI(Y) factors, STAT factors and pocket domain factors.
15. The method of claim 11, wherein said transcription factor is Egr-1.
16. The method of claim 11, wherein at least one cell or at least one nucleus is at least one cell.

17. The method of claim 16, wherein at least one cell is at least one living cell.
18. The method of claim 17, wherein said at least one living cell is irradiated prior to said cross-linking.
19. The method of claim 11, wherein said cross-linking is performed using formaldehyde.
20. A method for identifying one or more genes or DNA sequences regulated by a transcription factor, comprising:
- a) cross-linking at least one transcription factor to at least one nucleic acid molecule in at least one cell or at least one nucleus, forming one or more transcription factor-nucleic acid molecule complexes;
 - b) fragmenting said at least one nucleic acid molecule to form one or more transcription factor-nucleic acid molecule fragment complexes;
 - c) isolating one or more nucleic acid molecule fragments from said one or more transcription factor-nucleic acid molecule fragment complexes to obtain one or more isolated nucleic acid molecule fragments;
 - d) hybridizing said one or more isolated nucleic acid fragments to a known complementary nucleic acid sequence in an array of sequences known to be complementary to previously identified nucleic acid molecules of known sequence; and
- identifying one or more genes or DNA sequences regulated by a transcription factor when said one or more genes or DNA sequences regulated by a transcription factor hybridizes to said one or more isolated nucleic acid fragments on said array.
21. The method of claim 20, further comprising amplifying said one or more isolated nucleic acid molecule fragments prior to said hybridizing.
22. The method of claim 20, wherein said at least one nucleic acid molecule comprises genomic DNA.
23. The method of claim 20, wherein said one or more isolated isolated nucleic acid fragments comprise at least a portion of a gene operably linked to or in close

proximity to a nucleic acid sequence that binds with at least one transcription factor.

24. The method of claim 49, wherein said transcription factor is selected from the group consisting of leucine zipper factors, helix-loop-helix factors, helix-loop-helix/leucine zipper factors, NF-1 factors, RF-X factors, bHSH factors, Cys4 zinc finger of nuclear receptor factors, diverse Cys4 zinc finger factors, Cys2His2 zinc finger factors, Cys6 cysteine-zinc cluster factors, Homeo domain factors, paired box factors, fork head/winged helix factors, heat shock factors, tryptophane cluster factors, TEA domain factors, RHR factors, p53 factors, MADS box factors, beta-barrel alpha-helix factors, TATA-binding factors, HMG factors, heteromeric CCAAT factors, Grainyhead factors, cold-shock domain factors, Runt factors, copper fist factors, HMGI(Y) factors, STAT factors and pocket domain factors.
25. The method of claim 20, wherein said transcription factor is Egr-1.
26. The method of claim 20, wherein at least one cell or at least one nucleus is at least one cell.
27. The method of claim 26, wherein at least one cell is at least one living cell.
28. The method of claim 27, wherein at least one living cell is irradiated prior to said cross-linking.
29. The method of claim 22, wherein said cross-linking is performed using formaldehyde.
30. A composition having the DNA sequence (SEQ ID NO 27).
31. A composition having the amino acid sequence (SEQ ID NO 26).